

We Claim:

1. A method for protecting neuronal cells from degeneration in response to a neuronal insult, comprising intravenous administration to an animal in need thereof, a pharmaceutically effective amount of the tripeptide Gly-Pro-Glu (GPE).
- 5 2. The method of claim 1, wherein said GPE is administered as an infusion without a prior bolus injection.
3. The method of claim 1, wherein said GPE is administered as a bolus followed by an infusion.
4. The method of claim 1, wherein said GPE is administered from about 1 hours to  
10 about 24 hours after said neuronal insult.
5. A method for providing prolonged protection of neural cells from degeneration in an animal following a neuronal insult, comprising administering GPE to said animal via intravenous administration, said administration beginning from about 1 hour after the insult to about 24 hours after the insult.
- 15 6. A method of decreasing neural cell death or degeneration following a neuronal insult resulting from hypoxia/ischemia caused elective surgery, comprising administering GPE as an intravenous infusion over a duration of from about 1 to about 4 hours, said infusion beginning at a time from about 1 hour before to about 24 hours after said elective surgery.
7. A method of decreasing neural cell death or degeneration following a neuronal insult  
20 resulting from hypoxia/ischemia caused by stroke, comprising administering GPE as an intravenous infusion beginning at a time from about the onset of said stroke to about 24 hours after said stroke.
8. The method of claim 6, wherein said surgery is coronary artery bypass surgery.
9. The method of any of claims 1-8, wherein said GPE is administered in a  
25 pharmaceutically acceptable formulation.

10. The method of claim 3, wherein said GPE is administered as a bolus at a dose of about 0.03 mg/kg to about 30 mg/kg.
11. The method of any of claims 1-3, wherein said GPE is infused at a rate of about 0.03 mg/kg/h to about 30 mg/kg/h.
- 5 12. The method of any of claims 1-11, wherein said GPE is administered between about 1 to 7 hours after an insult that would otherwise result in neural degeneration or neuronal cell death.
13. The method of any of claims 1-11, wherein said GPE is administered between about 1 to about 11 h after an insult that would otherwise result in neural degeneration or neuronal  
10 cell death.
14. The method of claim 3, wherein the dose of GPE administered in said bolus is in the range of about 0.03 mg/kg to about 30 mg/kg, and wherein said GPE in said infusion is administered at a rate of about 0.03 mg/kg/h to about 30 mg/kg/h.
- 15 15. The method of claim 3, wherein the dose of GPE administered in said bolus is about 3 mg/kg and wherein said GPE in said infusion is administered at a rate of about 3 mg/kg/hr.
16. The method of claim 2, wherein said GPE is infused at a rate of about 0.3 mg/kg to about 3 mg/kg.
17. The method of any of claims 1-16, wherein said insult is a condition selected from the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, multiple  
20 sclerosis, amyotrophic lateral sclerosis, peripheral neuropathy, spinal muscular atrophy, Creutzfeldt-Jakob disease, AIDS dementia, progressive supranuclear palsy, myelinopathia centralis diffusa (vanishing white matter disease), chronic neurodegenerative disease, Down's syndrome, leukoencephalopathy, hypoxia, ischemia, coronary artery bypass graft (CABG) surgery and Schilder's disease, neuroblastoma, head injury, traumatic brain injury, stroke,  
25 reperfusion injury, epilepsy, toxin damage, radiation damage, asphyxia, an inflammatory condition, chronic or acute encephalomyelitis, encephalitis, optic neuritis, transverse myelitis, meningitis, panencephalitis, Devic's disease, progressive multifocal leukoencephalopathy, central pontine myelinolysis, depression, schizophrenia and neuromyelitis optica.

18. The method of any of claims 1-17, further comprising administering an additional neuroprotective agent.
19. The method of any of claims 1-18, wherein said additional neuroprotective agent is an anti-apoptotic agent or an anti-necrotic agent.
20. The method of claim 18, wherein said additional neuroprotective agent is selected from the group consisting of growth factors and associated derivatives (insulin-like growth factor-I [IGF-I], insulin-like growth factor-II [IGF-II], transforming growth factor- $\beta$ 1, activin, growth hormone, nerve growth factor, growth hormone binding protein, IGF-binding proteins [especially IGFBP-3], basic fibroblast growth factor, acidic fibroblast growth factor, the hst/Kfgk gene product, FGF-3, FGF-4, FGF-6, keratinocyte growth factor, androgen-induced growth factor, int-2, fibroblast growth factor homologous factor-1 (FHF-1), FHF-2, FHF-3 and FHF-4, keratinocyte growth factor 2, glial-activating factor, FGF-10 and FGF-16, ciliary neurotrophic factor, brain derived growth factor, neurotrophin 3, neurotrophin 4, bone morphogenetic protein 2 [BMP-2], glial-cell line derived neurotrophic factor, activity-dependant neurotrophic factor, cytokine leukaemia inhibiting factor, oncostatin M, an interleukin,  $\alpha$ -interferon,  $\beta$ -interferon,  $\gamma$ -interferon, consensus interferon, TNF- $\alpha$ , clomethiazole; kynurenic acid, Semax, tacrolimus, L-threo-1-phenyl-2-decanoylamino-3-morpholino-1-propanol, adrenocorticotropin-(4-9) analogue [ORG 2766], dizolcipine [MK-801], selegiline, a glutamate antagonist selected from the group consisting of NPS1506, GV1505260, MK-801 and GV150526, an AMPA antagonist selected from the group consisting of 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(f)quinoxaline (NBQX), LY303070 and LY300164 and anti-inflammatory agent selected from the group consisting of an anti-MAdCAM-1 antibody and an antibody against an integrin  $\alpha$ 4 $\beta$ 1 receptor and an integrin  $\alpha$ 4 $\beta$ 7 receptor.
21. The method of claim 5, wherein said administration is carried out for a period of from about 1 to about 4 hours duration.
22. The method of any of claims 1-21, further comprising administration of an enzyme inhibitor capable of inhibiting the degradation of GPE in plasma.
23. The method of any of claims 1021, further comprising administration of one or more inhibitors of carboxypeptidases, aminopeptidases, peptidyl dipeptidases, metalloproteinases and dipeptidases.

24. The method of any of claims 1-21, further comprising administration of one or more enzyme inhibitors selected from the group consisting of aprotinin, pepstatin A, bestatin, leupeptin, AEBSF and E-64.

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25. A composition comprising:  
GPE; and  
at least one protease or peptidase inhibitor.

10 26. The composition of claim 26, wherein said inhibitor is capable of inhibiting a serine protease, a carboxypeptidase, an aminopeptidase, a cysteine protease, a dipeptidyl peptidase, a metalloprotease and/or a peptidyl dipeptidase.

15 27. The composition of claim 25, wherein said at least one protease or peptidase inhibitor is selected from the group consisting of aprotinin, a metalloproteinase inhibitor, pepstatin A, bestatin, leupeptin, AEBSF and E-64.

28. The composition of any of claims 25-27 further comprising a pharmaceutically acceptable excipient.

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